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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,152	02/01/2001	Chris C. Miller	RR-473PCT/US	1414

7590 04/16/2004

SAMUEL N. Tiu, Esq.
SIDLEY AUSTIN BROWN & Wood
555 West Fifth Street
Los Angeles, CA 90013-1010

EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,152	MILLER, CHRIS C.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 70-84 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 70-84 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/03/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of amendments and IDS filed 12/03/03 and the supplemental amendment filed 01/02/04.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 12/03/03 is considered by the examiner. Documents listed under Additional Information (sheet 3 of 3) were considered, but since they are not considered prior art and can not be published as such, will not be initialed on PTO-1449.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 70-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (WO 9509612) in view of Bathe et al (5,558,083).

Green teaches compositions capable of releasing nitric oxide and therapeutic methods of use thereof for the treatment of microorganism-related disease states. It is discloses that direct delivery of nitric oxide gas kills intracellular pathogens such as *Mycobacterium tuberculosis*. An ability to specifically deliver compounds capable of releasing nitric oxide to the desired site of infection within the macrophage would greatly enhance killing of intracellular pathogens (page 5, lines 6-13).

Green discloses a method of inhibiting the proliferation of parasites, fungi, bacteria and other proliferating cells or organisms (page 7, lines 30-34). Also disclosed is that the nitric oxide releasing compounds, alone or in combination with other suitable components, can be made into aerosol formulations to be administered via inhalation (page 23, lines 7-10). *Administration through the aerosol route is highly beneficial* to humans or animals with pulmonary infections. Various bacterial, protozoan, fungal, viral and parasitic infections of the respiratory system that involve macrophages are attacked in this fashion (page 29, lines 15-25).

Green discloses that the dose administered to an animal, particularly a human, should be sufficient to effect a therapeutic response in the animal over reasonable time frame (page 24, line 30 to page 24, line 12). Greene lacks specific disclosure on diluting nitric oxide with air and flow-controlled delivery.

Bathe et al teaches a nitric oxide delivery system that is useable with any of a variety of gas delivery system that provides breathing gas to a patient. Nitric oxide in a diluent gas is delivered from a gas control valve (see abstract).

Bathe discloses that nitric oxide is delivered using systems such as ventilation, where the NO is introduced by means of a gas proportioning device that provides a continuous flow to the patient. The invention includes a flow transducer that senses the flow of gas from the gas delivery system (col. 2, lines 13-30).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the method of killing and inhibiting the proliferation of extracellular microorganisms within the respiratory system of an animal by implementing the flow-controlled and diluted delivery system of Bethe et al because as disclosed nitric oxide can be toxic at certain concentrations and therefore its delivery should be monitored and calculated. Greene does not specifically disclose a method of suppressing a respiratory infection associated with microorganisms, however, method of killing and inhibition are disclosed and clearly killing the microorganism leads to suppressing the infection. It is also noted that the method of delivery and the population are the same in both methods of claims 70 and 79. One of ordinary skill in the art would clearly be led to conclude that the same criteria can be effective in suppression of the infection.

Response to Arguments

Applicant's arguments with respect to claims 14, 19-30 and 42-55 have been considered but are moot in view of the new ground(s) of rejection. However, since Greene et al is the primary reference in the new rejection arguments regarding the said reference will be addressed.

Applicant argues that "Green does not disclose the inhalation of nitric oxide gas for killing, inhibiting or suppressing pathogenic microorganisms, as claimed by Applicant". This is not correct. Greene is clearly disclosing a method of killing or

inhibiting the proliferation of infectious or pathogenic microorganisms in animals (see page 7, last paragraph and claim 1).

Applicant argues that Greene is disclosing compounds capable of releasing nitric oxide in aqueous solution rather than delivery of nitric oxide gas itself through inhalation. This is not commensurate with the scope of the claims. The instant claims do not require a delivery of nitric oxide gas directly to the respiratory system. In fact claims 70 and 79 recite "source of nitric oxide" and claim 76 recites "a nitric oxide substrate source containing a compound capable of producing nitric oxide". The specification also discloses that "nitric oxide source may be a compound, composition or substance producing nitric oxide" (see page 6, lines 7-8).

Applicant argues that Greene does not teach the delivery of gaseous nitric oxide through inhalation. This is not commensurate with the scope of the claims. Instant claims require a source of nitric oxide and Greene is disclosing a compound releasing nitric oxide gas directly onto the microorganism, which clearly meets the limitation of instant claims. Greene also discloses that "the nitric oxide releasing compounds, alone or in combination wit other suitable compounds, can be made into aerosol formulations to be administered via inhalation. These aerosol formulations can be placed into pressurized acceptable propellants" (see page 23, 2nd paragraph). Inhalation is also clearly disclosed in page 29, lines 15-25, where it is disclosed that pulmonary delivery is beneficial to humans or animals with pulmonary infections.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mina Haghighatian
April 06, 2004

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600